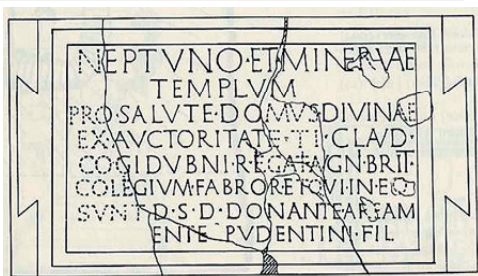


On reaching 150

Bandolier sometimes feels old, just as if we have been dug out of the ground and found as in inscription for future generations to scratch their heads over. There is a Churchillian expression that sums up our attitude to life. A small prize for the first person to email in what the expression may be.



On taking things on trust

We take an awful lot of things on trust. Of course, some of us have more acutely tuned antennae for spotting nonsense than others, and Bandolier is all about spotting it, which is why we've even tuned it into a book.

Times columnist Matthew Parris decided to source the barrage of advice about turning off electrical units on standby, a supposed major cause of wasted electricity. Little red lights wasted up to 10% of the electricity supply, or 1% of global carbon emissions. This was big. Even Andrew's mother's hairdresser's friend knew about it, and religiously turned everything off.

Matthew tracked down a review of the topic [1], and was astonished to find that UK data was from a single study in only 32 homes. Whole-house measurements of standby power use in 21 studies had examined between 1 and 178 homes. But worldwide results were pretty consistent, with annual standby use of 300-1000 kWh/year. The UK figure averaged 280 kWh/year, supposedly 8% of total residential electricity use, though in Bandolier's mean (both meanings) pad it would be half that. Another review [2] estimates standby power uses 1.5% of all electricity consumption in OECD countries: a small percentage but an awful lot of power.

Redesigning circuits could reduce standby power consumption by 90%. Standby power use by individual appliances varies up to 20-fold. The message is not just about taking figures on trust, but governments getting a grip on what is known doing something, rather than just bleating at us.

- 1 AK Meier. A worldwide review of standby power use in homes. 2001 Lawrence Berkeley National Laboratory. Paper LBNL-49377: repositories.cdlib.org/lbnl/LBNL-49377.
- 2 B Mohanty. Standby power losses in household electrical appliances and office equipment. Presented in 2001.

Bandolier's Little Book of Making Sense of the Medical Evidence

Bandolier is delighted to announce that its little book of making sense of the medical evidence has been published by Oxford University Press. It provides practical guidelines on how to make sense of and interpret available evidence, with information on how to avoid straying beyond evidence into conjecture, supposition, and wishful thinking. It covers size, trial design, harm as well as benefit, from randomised trials and observational studies, and includes as well information about diagnostic testing, health economics, and management evidence.

The book's origins lie in lectures for medical students, healthcare professionals, and journalists. It was not written as a comprehensive manual for those who want to do a systematic review or meta-analysis, nor as a statistical or methodological textbook. Rather, summarises tools Bandolier uses to assess evidence, to be able to distinguish good evidence from bad. It will (hopefully) be an invaluable resource for university course and GP tutors, family doctors, hospital consultants involved in research, pharmacists, and anyone interested in evidence-based health care.

Why did we write it? Reasons stem from writing 150 issues of Bandolier, trying to get our brains around why things seem so complicated, and then trying to explain it simply to others. We have been helped by being intimately involved in over 100 systematic reviews in different areas, and trying to get to grips with some of the methodological complexities that can help, and sometimes hinder.

Much wool is being pulled over many eyes, and from many different directions. Our working theme was one of bullshit detection. If it helps some of you become bullshit detectors, then we will be happy with that result. Buy it if you like, but it won't make Bandolier rich.

Available from Oxford University Press
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2006 / 440 pp / 164 illustrations

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DOES SMOKING MARIJUANA CAUSE LUNG CANCER?

One might well think so. We know that burning plant products produces smoke, which contains tars, carcinogens, and other unpleasant compounds. We know that breathing smoke gets these materials deep into our lungs – which is why, in part, inhaling drugs can be an important option for drug delivery. We know that breathing smoke regularly, as in cigarette and other tobacco smoking, leads to increased rates of lung cancer, in a dose dependent manner. OK, we don't have much in the way of randomised trials in humans, but we have mountains of observational data.

So our starting point is to expect marijuana smoking to cause cancer, by simple analogy. But some might want the evidence for this, which is where it gets complicated. A systematic review [1] helps, because it has looked for evidence from various sources to test the biological plausibility that smoking marijuana causes lung cancer.

Systematic review [1]

The review used a broad search strategy for experimental studies of any design published up to the end of 2005, but only in English. The 19 that were finally included were divided into which relationship was investigated between marijuana smoking and possible lung cancer.

Results

These are summarised in Table 1. Five general areas were examined, the relationship between marijuana smoking and exposure to tar, cytology of sputum, changes in alveolar macrophages and bronchial biopsies, and epidemiological studies examining lung cancer or related conditions.

Smoking marijuana led to increased tar delivery, more cellular changes in sputum, damage to alveolar macrophages,

and increased abnormality in bronchial biopsies, with increased surrogate markers for lung cancer.

The epidemiological studies did not find any consistent relationship between marijuana smoking and cancer of all sites, though the bulk of the participants were from a retrospective review of a health plan from the early 1980s. Small studies of a few hundred patients indicated non-significant increases in lung cancer with marijuana smoking.

Comment

There is abundant circumstantial evidence pointing to a plausible biological relationship between marijuana smoking and lung cancer. We may be lacking the smoking gun, but few juries could fail to convict on this evidence.

We have the advantage of knowing that consistent smoke inhalation, whether tobacco, marijuana, or anything else, is a really bad thing. For instance, the high incidence of lung cancer among non-smoking Chinese women in Hong Kong has been linked, at least in part, to cooking fumes associated with frying [2]. Smoke in wildland fires in the USA has at least 15 carcinogens, and risk assessment for firefighters with chronic smoke exposure includes a significant excess of cancers [3]. This allows us to be even more certain of a probable link between marijuana smoking and lung cancer, and not to be too hung up about wanting more evidence.

References:

- 1 R Mehra et al. The association between marijuana smoking and lung cancer. A systematic review. Archives of Internal Medicine 2006 166: 1359-1367.
- 2 IT Yu et al. Dose-relationship between cooking fumes exposures and lung cancer among Chinese non-smoking women. Cancer Research 2006 66: 4961-4967.
- 3 TF Booze et al. A screening-level assessment of the health risks of chronic smoke exposure for wildland firefighters. Journal of Occupational and Environmental Hygiene 2004 1: 296-305.

Table 1: Summary of studies of association between marijuana smoking and lung cancer

Type of study	Number	Synopsis
Exposure to tar	4 experimental studies with 45 participants	Smoking marijuana is associated with increased tar delivery to the lungs, to a greater extent than smoking cigarettes, perhaps by a factor of three
Cytomorphology of sputum samples	2 studies with 150 participants	Marijuana smokers who did not use tobacco had more metaplastic cells, pigmented macrophages and columnar cells than nonsmokers. Dysplasia in 0% of non-smokers, but 12% and 4% of tobacco or marijuana smokers
Alveolar macrophage changes	3 studies with 128 participants	Alveolar macrophages from marijuana smokers had less tumoricidal ability, enhanced oxidative stress, and a dose-dependent relationship between THC and reactive oxygen species. Possibly increased DNA damage
Histopathology and molecular alterations in bronchial biopsies	6 studies with 494 participants undergoing bronchoscopy	Increase in abnormal and precancerous findings in marijuana smokers compared with tobacco smokers. Surrogate markers for lung malignancy more often found in marijuana smokers
Lung cancer or related outcomes	4 studies with 65,000 participants, predominantly in a single study	No relationship between marijuana smoking and diagnosis of lung cancer. Limited evidence of higher use of marijuana in younger patients with lung cancer

STATINS AND ALBUMINURIA

There are times when you just don't know what to think of evidence, especially when it comes on a topic that one's tired mind has not considered before. Is it overwhelming, underwhelming, or something in between? A systematic review [1] looking at the effects of statins on urinary albumin or protein excretion is a useful example of how to look at evidence, over and above being of interest in itself.

Systematic review

Many databases were searched for randomised studies in adults of statin compared with placebo, with urinary excretion of albumin or protein as an outcome. Information required was the mean baseline and final excretion rates for statin and placebo groups. Prior intent was to analyse according to the level of albumin or protein excretion, with below 30 mg/day as normal excretion, between 30 and 299 mg/day as microalbuminuria, and 300 mg/day or more being macroalbuminuria.

Results

Fifteen trials with 1,384 participants were found. Three trials with 938 patients had normal urinary albumin excretion (based on average of all patients), six (171 patients) had microalbuminuria, and six (275 patients) had macroalbuminuria or proteinuria above 300 mg/day. Two of the trials were not double blind, and one had no clear eligibility criteria.

There was clinical heterogeneity between studies, with causes of raised albumin including diabetes, IgA nephropathy,

hypertension, and complex kidney disease, or not being reported in one trial. There was one large trial, but most were small, with only eight patients treated with statins in two trials. Trial duration was three to 46 months, with most between three and 12 months.

The results of the statin treatment arms in individual trials are shown in Figure 1, using a logarithmic scale because baseline excretion varied between <10 mg/day and more than 5,000 mg/day.

With placebo, urinary albumin or protein excretion changed but little. No trial where baseline urinary albumin excretion was normal had any meaningful change in excretion with statin. Most trials where patients had raised baseline urinary albumin excretion showed substantial reductions with statin treatment.

The weighted mean percentage reduction was about 50% for both microalbuminuria and macroalbuminuria or raised protein excretion compared with placebo. The exceptions were two trials. One was neither double blind nor had clear eligibility criteria in 36 patients with type 2 diabetes and apparently a mean age of 24 years. The second was in 30 patients with complex renal problems.

Comment

The authors of the paper do a good job of making sense of their data, but perhaps miss the obvious problem when assessing an outcome of urinary albumin excretion. For instance, if an excretion is reported as 5,000 mg/day, with a standard deviation of 2,500 mg/day, the chances are that data used for these calculations are not normally distributed. Some individual urinary excretions could be very high, while many could be lower; in the circumstance an average may not be representative of urinary excretion values of most patients.

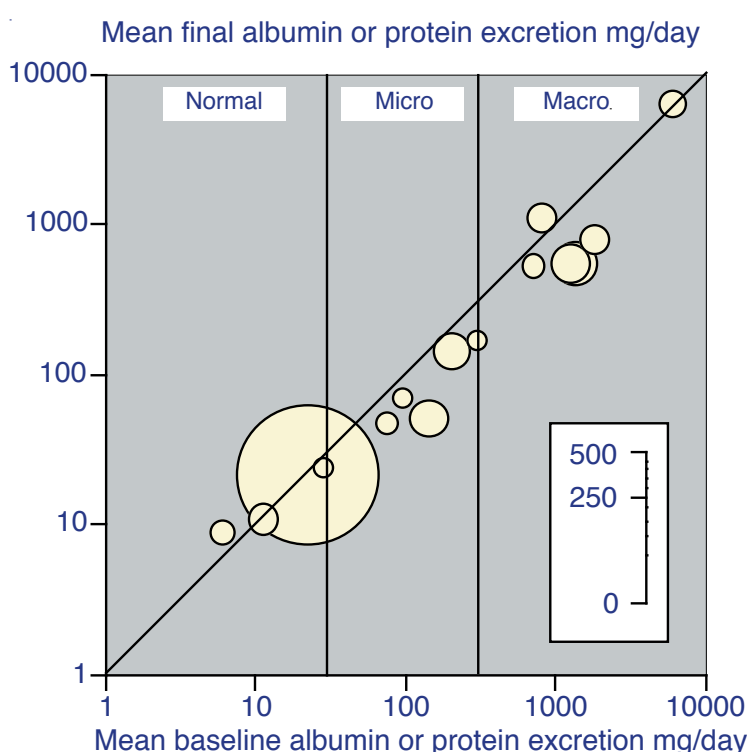
Is the mean meaningful, in that case? It probably is much less useful than a median, and the mean may mislead. The fact that we see means falling by 50% in most trials should therefore give us some confidence, because results are consistent. Moreover, the two trials not in overall agreement are one with the lowest quality, and the only one in complex kidney disease, quite different from the others.

However, this is an excellent example about how one could lose a potentially important effect by lumping together clinically heterogeneous groups. Almost 70% of participants had normal urine protein excretion, and here there was no change. Had the analysis lumped these together with those with increased urine protein excretion, the effect may have been missed. It emphasises that we need always to ask the question whether these patients in the trial are like ours, and always to ask for the most appropriate analysis of data.

Reference:

- 1 K Douglas et al. Meta-analysis: the effect of statins on albuminuria. *Annals of Internal Medicine* 2006 145: 117-124.

Figure 1: Individual studies showing baseline and final urinary albumin excretion, by normal albumin excretion, and micro- and macroalbuminuria



SUDDEN CARDIAC DEATH

It becomes obvious when one begins to write about risk, as Bandolier has been doing in recent issues, that some sort of background is needed. Risk examines mainly serious consequences, most often death. While Keynes' dictum about us all being dead in the long run is all very well, it is the short run that we worry about most.

So what is the chance of us dying tomorrow, from anything, or from something? Figure 1 shows UK data on mortality from 2003, by age and by sex. It tells us what we already know, that our risk of dying increases as we get older, and is higher for men (filled symbols) than women (open symbols) at almost all ages. Of course, these are averages, and people leading healthy lifestyles are likely always to have lower risk than those who do not.

What about looking at particular causes of death? Governments produce lots of useful information, and in the UK there have been impressive reductions since 1979 in death rates for both sexes, at almost all ages, but especially in middle age, and from many causes. But if we want answers to more specific questions, we have turn to the epidemiologists. So let's look at sudden cardiac death, where definitions have changed in recent years, with the time interval between onset of symptoms and death reduced from 24 to one hour.

Study

The study [1] was conducted in Holland using an electronic database of about 500,000 people registered with a general practitioner. The records contain coded comprehensive and anonymous data that allows for epidemiological studies. In this case the study was over six years, from 1995 to 2001, in people aged 18 years or older, registered for at least one

Figure 1: Risk of death in UK by age and sex, for 2003.
Open symbols, women; solid circles, men

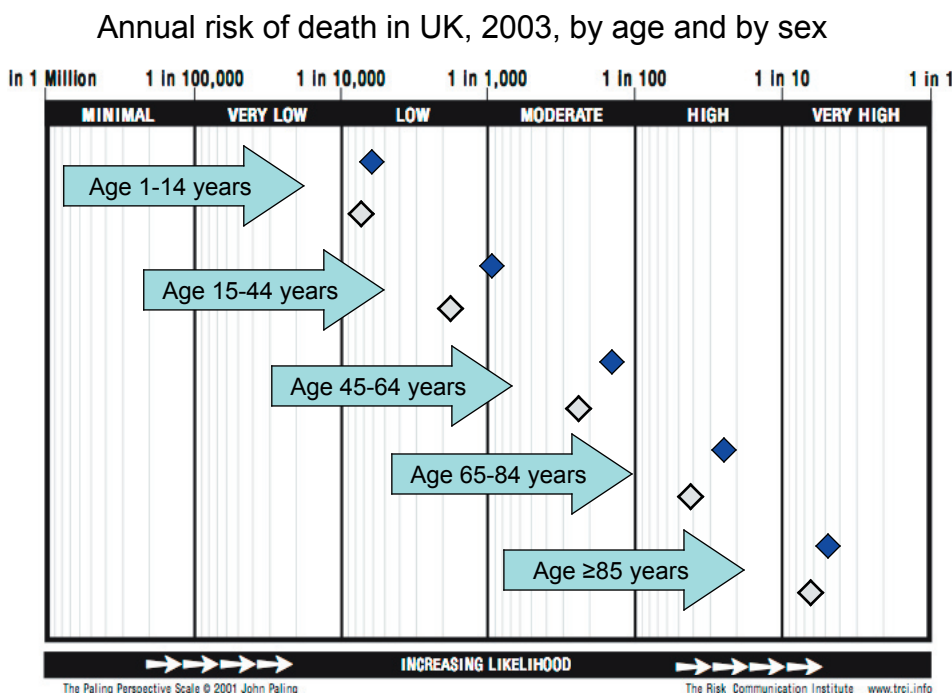
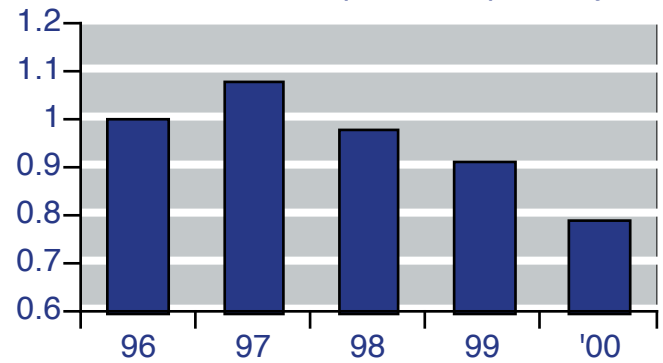


Figure 2: Incidence of sudden cardiac death in Holland, by year

Sudden cardiac death, per 1,000 person years



year. Medical records of all deaths were examined to classify the circumstances, whether the death could be classified as cardiac, and whether people were previously in good health. Only deaths from suicide and in patients with cancer were excluded from examination.

Results

The final population was 250,000 people, with a median age of 40 years, and 51% female. There were 4,892 deaths, of which 582 (12%) were probable sudden cardiac deaths. The median age of cases was 72 years, with 59% male. The median age of male cases was 70 years, compared with 76 years for female cases.

Sudden death was witnessed in 354 cases, with 76% occurring in the home, 14% in a public place and 5% in an ambulance or on arrival at hospital. In the 228 unwitnessed cases, the majority occurred at home when a place was mentioned.

The incidence of sudden cardiac death declined slightly over the period (Figure 2). The incidence increased with age in women and men (Figure 3), with and age adjusted rate of 2.3.

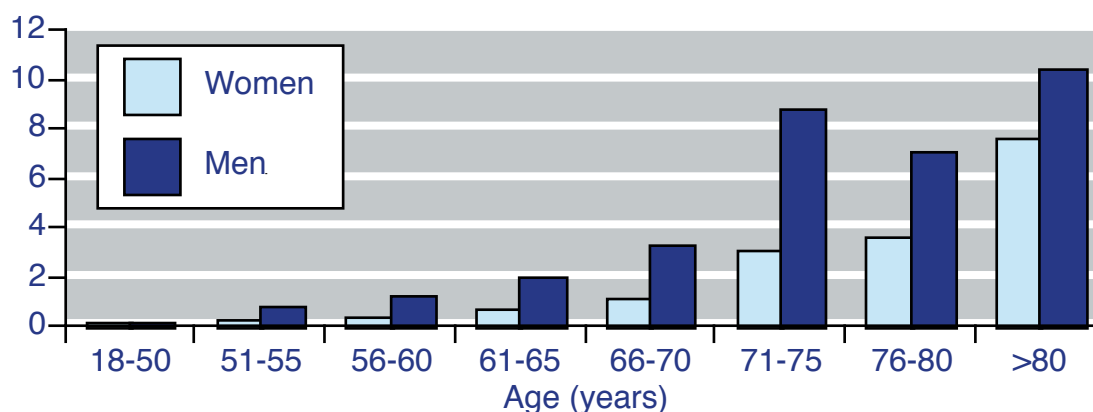
The incidence was highest in October, and lowest in August, with more cases on Mondays and Tuesdays than Thursdays.

Comment

As always, it is useful to recognise that stuff happens. Whoever and wherever we are, bad things can come out of that blue sky, sometimes without any warning. For men over the age of 70 years, 1 in 100 are likely to have a sudden cardiac death each year. For men in their 60s, sudden cardiac death runs at about 2 per 1000, or 1 in 500. That is 40 times more likely than being killed in a road traffic accident.

So if we put our seat belts on when we drive to keep us safe, and avoid doing crazy things on the road, it makes even

Figure 3: Incidence of sudden cardiac death in Holland, by age and sex
Sudden cardiac death, per 1,000 person years



more sense to avoid doing crazy things with our hearts. Not smoking, eating healthily, and a modicum of exercise and alcohol makes sense, really. If a behaviour is less risky than driving (chance of dying 1 in 20,000 per year) we probably accept it. Having an unhealthy lifestyle is much, much, more risky than that.

Reference:

- 1 SM Straus et al. The incidence of sudden cardiac death in the general population. *Journal of Clinical Epidemiology* 2004 57: 98-102.

MOSQUITO REPELLENT EVIDENCE



Avoiding being bitten by mosquitoes or other little nasties is usually about preventing discomfort in the short or medium term. Because those little nasties can sometimes be vectors of several unpleasant diseases in different parts of the world, though, it can be more important than that. So, as one Bandolier reader asked, what's the evidence for which repellent works best?

This is not quite so easy to answer as one might think, because the number of variables is legion. The mosquito, for a start. It's sex, the number of them, how hungry they are, the temperature, humidity, and wind speed can all affect the likelihood of being bitten, with or without any repellent present. So controlled laboratory tests are the order of the day, and the best is a study looking at 16 different repellents tested in 15 intrepid volunteers in controlled circumstances [1].

The test

Basically, the test comprised one arm being placed in a cage containing a fixed number of unfed mosquitoes and measuring how long it took until the first bite. Cages contained 10 disease-free female *Aedes aegypti* mosquitoes between seven and 24 days old, reared in a laboratory, and not previously exposed to a repellent. Temperature, humidity and light-dark cycles were controlled.

Before each test, the readiness of mosquitoes to bite was measured by inserting an untreated arm, and observing five mosquito landings on the arm. Repellent was then applied (or worn in the case of wristbands), and the arm reinserted, according to a set schedule.

Simply, this started with insertion of the treated arm for one minute in every five for the first 20 minutes, then one minute every 15 minutes until the first bite, the time of which

Table 1: Complete protection time against mosquito bite

Active ingredient	Mean complete protection time (minutes)
Synthetics	
DEET, 24%	302
DEET, 20%	234
DEET, 6.7%	112
DEET, 4.8%	88
IR3535, 7.5%	23
Natural products	
Soybean oil, 2%	95
Citronella, 10%	20
Citronella, 12% plus other oils	19
Citronella, 10% plus peppermint	14
Citronella, 5%	14
Citronella, 1% bath oil	10
Uncertain mix bath oil	10
Citronella, 0.05%	2.8
Wristbands	
DEET, 9.5% wristband	0.3
DEET, 9.5% wristband	0.2
Citronella, 25% wristband	0.2

Products were applied to the skin from elbow to fingertips, except wristbands.

was recorded. Each volunteer made three measures for each repellent. This was done for each of 16 commercially obtained products. The order of testing was determined by a random number generator for each subject.

Results

The results are shown in Table 1. Certain results are obvious.

- No wristband worked.
- Natural products or oils were ineffective, except for about 1.5 hours of protection with a product containing soybean oil.
- The European product IR3535 was ineffective.
- DEET at higher concentrations applied to the skin provided up to five hours of complete protection against mosquito bites.

Comment

This paper tested 16 products available commercially in the USA. It was one of those studies, beautifully done, that did not need statistics. The answer was obvious.

But all may not be up for natural products, or different products available in different countries, though we could not find any that had been tested in the same stringent way. For instance, testing of 38 essential oils in laboratory conditions found that only four (citronella, patchuli, clove, and makaen) gave two hours protection, and only at 100% concentration [2]. Diluted to 50% or 10%, they were largely ineffective, echoing the US findings [1]. However, three commercially available products in South Africa (one with 15% DEET, one with another synthetic agent, and one containing a mixture of oils) all produced 3-4 hours of almost complete protection, though the natural oil product declined rapidly after that time [3].

Undoubtedly there is more literature than this, but right now, unless there is good data to show that another product works, choosing DEET repellent products is the sensible and safe thing to do. For travellers, the Centres for Disease Control has much useful advice about general preventative measures and repellents, at www2.ncid.cdc.gov/travel (look for the yellow book section). The main points are:

- Use repellent on exposed skin, but not on cuts, wounds, or irritated skin. Wash off repellent when you come indoors again.
- Avoid known foci of disease transmission. Simple changes in itinerary can greatly reduce risk. Avoid times when mosquitoes are most active, in twilight for instance.
- Wear long sleeved shirts, long trousers, minimise exposed skin. Tuck trousers into socks.
- Use bed nets and gear with repellents.

References:

- 1 MS Fradin, JF Day. Comparative efficacy of insect repellents against mosquito bites. *NEJM* 2002 347: 13-18.
- 2 Y Trongtokit et al. Comparative repellency of 38 essential oils against mosquito bites. *Phytotherapy Research* 2005 19: 303-309.
- 3 J Govere et al. Efficacy of three insect repellents against the malaria vector *Anopheles arabiensis*. *Medical and Veterinary Entomology* 2000 14: 441-444.

INDUSTRY BIAS IN CLINICAL TRIALS?

We have become used to finding potential sources of bias in clinical trials. What we find is usually empirical evidence of bias from some examples, and then we look for the possibility that bias from that particular source might be affecting other results we are considering. If there is sufficient information, we might test whether that bias exists in our data using a sensitivity analysis. As a simple example, we might test randomised or double blind studies against those that are not randomised or double blind.

Industry bias

The majority of clinical and laboratory work undertaken is funded by industry, small or large. Concerns have been expressed about whether this can lead to bias, and there is a considerable, if somewhat confused, literature. In part this is because at least two possible issues come under this heading:

- 1 Marketing bias. Companies want to present their products in the best possible light, and will be selective about what they say. This applies to small spin-offs looking for development capital, to large organisations seeking to market new pharmaceuticals, tests, or devices.
- 2 Sponsorship bias. Narrowly defined, this is whether the source of funding for a clinical trial affects the results of the clinical trials in a systematic way.

The existence of marketing bias would be conceded universally. It is part of the world we work in. You don't see adverts, for instance, saying that margarine tastes worse than butter. Every book on the bookstand is an international best seller.

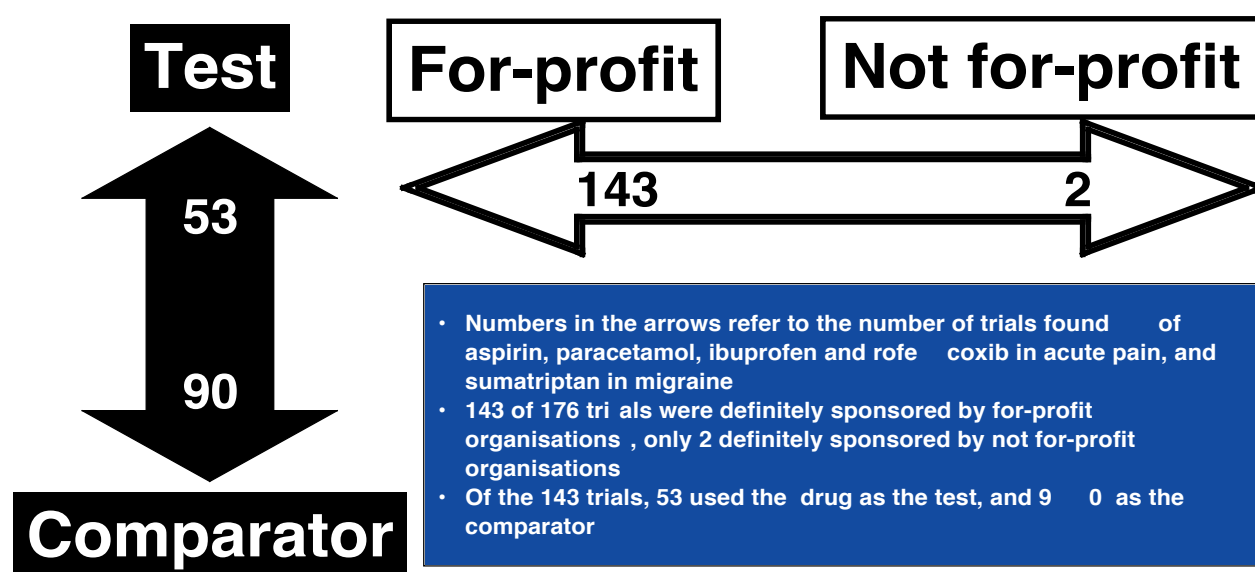
Whether sponsorship bias exists, though, is another matter. Although there have been many reviews claiming the existence of industry bias, these have typically made a heap of what they could find, irrespective of criteria of quality, validity, and size, and have typically not compared like with like. A new systematic review [1] is possibly the first to look specifically at whether sponsorship bias exists in clinical trials, and gives a useful summary of some of the reviews that claim to have found industry bias.

Review

The review used existing meta-analyses of high quality acute pain and migraine interventions, which had chosen randomised and double blind trials that were valid, used a defined dose, and used consistent methods, had the same outcomes measured over the same time, and where there was a large amount of information. These were oral aspirin 600/650 mg, paracetamol 1000 mg, ibuprofen 400 mg and rofecoxib 50 mg in acute pain, and oral sumatriptan 100 mg and 50 mg for migraine; all were compared with placebo.

The intention was to compare efficacy in trials sponsored by for-profit organisations with those without for-profit sponsorship.

Figure 1: Strategy for examining the existence of differential sponsorship bias in randomised trials in acute pain and migraine where source of sponsorship was definite



Results

Of 176 individual trials, only two could be identified as being definitely sponsored by non-profit sources, compared with 144 sponsored by for-profit sources. No statement was made in 31 trials. Clearly no comparison between for-profit and not for-profit sponsorship was possible.

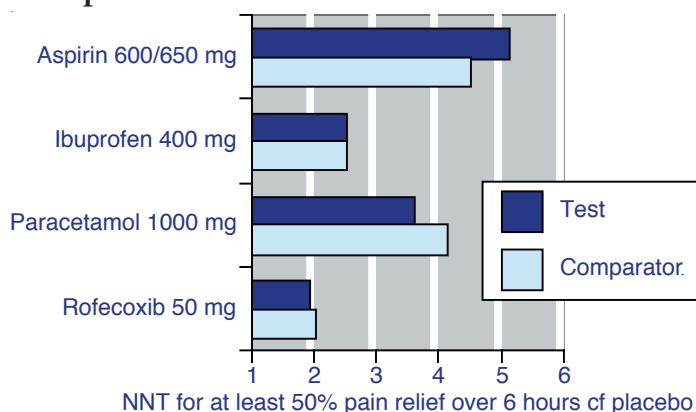
An alternative strategy was used (Figure 1). In the 143 for-profit trials, a distinction was made between trials where a drug was being used as a test, or as a comparator. The argument was that if bias existed, there would be conflicts of interest within industry-sponsored trials. The bias should act to maximise efficacy when a drug was used as the test drug (the aim being to make it look as good as possible), and to minimise efficacy when the same drug was used as a comparator (the aim being to minimise efficacy compared to a second, newer, test drug).

When this strategy was applied to four analgesics in acute pain trials, no difference in efficacy was found (Figure 2) as measured by the NNT for at least half pain relief over 4-6 hours compared with placebo. For sumatriptan in acute migraine, there were no consistent differences at 50 mg or 100 mg, for three different outcomes.

Comment

The conclusion here was that the only way of testing these studies was to look for differential sponsorship bias. When sought, no bias was found. It looks very much as if for-profit industry sponsorship does not influence the outcome of good quality, randomised trials in acute pain and migraine. There are also examples of large, high quality for-profit and not for-profit sponsorship trials of statins and finasteride giving essentially the same result.

Figure 2: NNT for four analgesics in identical randomised, double blind acute pain trials reporting the same outcome over the same period of time, where drug was used as test or comparator



This is very good news, and should be looked at in other areas. Had differential sponsorship bias been found, it would mean that we would probably not be able to trust randomised trials, since almost all have for-profit sponsorship. That would have been a bit of a blow.

The paper [1] gives examples, though, of marketing bias, where individual trials with particular beneficial characteristics were picked out for special marketing attention. The lesson is to treat all sources of information, industry or other, as if they were used car salespeople trying to sell you a dud. Ask for the evidence, and accept only good evidence, not airy-fairy nonsense about contented customers. If they can't show it, it may be because there isn't any. Never mind the shine, look for the quality.

Reference:

- 1 J Barden et al. Bias from industry trial funding? A framework, a suggested approach, and a negative result. *Pain* 2006 121: 207-218.

COST EFFECTIVENESS OF BNP TESTING

Bandolier 149 examined a systematic review of the accuracy of BNP testing. It showed that in secondary care situations where about 50% of patients had heart failure according to gold standard diagnostic procedures, the test had reasonable accuracy, though that depended somewhat on the cut-off values set in individual studies. That leaves open the question of whether it is not only useful clinically, but whether also cost effective. A new randomised trial suggests that it is [1].

Trial

This was conducted on 452 patients presenting with acute dyspnoea to the emergency department of a Swiss university hospital. Trauma patients, and those with severe renal disease or cardiogenic shock were excluded. Randomisation was to a diagnostic strategy that included measurement of BNP, or a conventional diagnostic strategy.

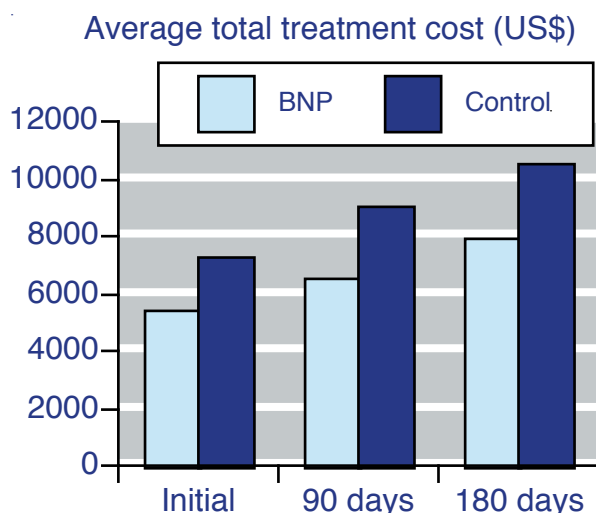
Two BNP cut-offs were used to separate heart failure from other causes of acute dyspnoea, less than 100 ng/L to rule out heart failure, and >500 ng/L to rule in heart failure. In this case rapid therapy with diuretics, nitroglycerin, and ACE inhibitors was recommended. Patients in the control group were examined and treated according to most recent guidelines.

Various outcomes were recorded over six months, including mortality, time in hospital, and costs. These were analysed for the initial hospital visit, and at 90 and 180 days.

Results

Patients had an average age of 71 years, about 40% were women, and they were comparable in terms of baseline characteristics. Follow up was complete in all but one patient.

Figure 1: Total treatment costs with emergency room BNP testing or conventional diagnostic strategy in patients admitted with acute dyspnoea



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Acute heart failure was the final discharge diagnosis in 45% in the BNP group and 51% in the control group, with exacerbated COPD or asthma in 23% and 11% respectively. In the BNP group, BNP levels were less than 100 ng/L in 36%, between 100 and 500 ng/L in 28%, and above 500 ng/L in 36%.

In patients in whom BNP had been used diagnostically, compared with the control group using standard diagnostic procedures, there was significantly less use of intensive care beds, 15% of patients compared with 24%, 10 vs 18 hours average use per patient, and 6% rather than 12% of patients required any ventilatory support. There was insignificant but consistently less use of echocardiography (40% vs 49%) and coronary angiography (5% vs 9%).

Patients in the BNP group required fewer days in hospital, 8 vs 10 following the initial visit, with a greater difference of 10 vs 14 days over 180 days. Initially and over 180 days, mortality was lower, by about 2 or 3 per 100 patients.

Total treatment costs were lower when BNP tests were used for the initial diagnosis, at all stages during the first 180 days (Figure 1). The average saving per patient initially was \$1,900, rising to \$2,600 over 180 days. Medication costs were the same, and most of the saving came from reduced use of hospital beds.

Comment

Isn't it terrific when it all comes together? If good systematic reviews of good studies of diagnostic tests are rare as hens' teeth (as in Bandolier 149), then good randomised trials of effectiveness with good cost information are even rarer. This formidable study from Switzerland even comes with modelling around how this looks in a cost-effectiveness plane looking at costs and mortality. Most of 5,000 simulations were in the dominant quadrant of lower cost and lower mortality with use of BNP tests in the emergency department.

A word of caution, though. This is a particular, and probably most important, use of BNP in secondary care. How the model would work in a primary care situation is something we do not yet know with the same degree of certainty. More thinking still needs to be done for that setting.

Reference:

- 1 C Mueller et al. Cost-effectiveness of B-type natriuretic peptide testing in patients with acute dyspnoea. Archives of Internal Medicine 2006 166: 1081-1087.